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Quality Specifications

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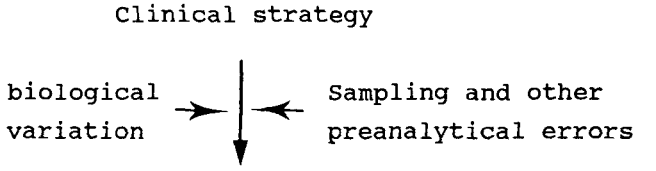
Use of analytical components in clinical strategies are decided without paying much attention to the quality of analytical performance, e.g. from Danish recommendations: 'in non-insuline dependent diabetics the clinical goal is to keep HbA_{1C} < 7.5 percent (1)' and 'guidelines for treatment of patients with P- Cholesterol (total) between 7 and 9 mmol/L (2)'. Influence from both biological and analytical variations seems to be forgotten or ignored, although the significances of these factors have been documented (3,4). Also sampling error and other preanalytical factors should be considered.

These are just examples, but they confirm the need for continuation of two previous NORDKEM projects on quality requirements (5) and quality control (6).

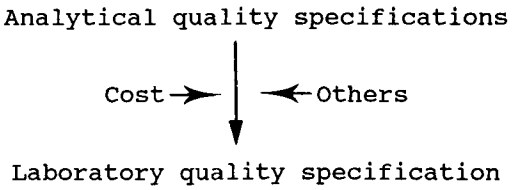


The needs for analytical quality are different for various clinical situations as demonstrated for TSH- measurements, where the quality needed for basal S-TSH determinations used 'to predict S-TSH response to TRH' is extremely demanding (7), whereas the requirements for B-TSH measurements in screening for congenital hypothyroidism are very loose (8). In these examples

the analytical procedure used for obtaining the quality required for 'predicting the S-TSH response' is very costly and should not be used for the screening of all newborns, where a simpler method is sufficient.

The analytical quality needed should be specified for each clinical strategy and the most demanding specifications should be aimed at when new methods and equipments are introduced - also when control systems is designed (6).

In practice costs, turn around-time, and other factors may interfere in obtaining the needed quality must not be forgotten, and should be the goal for later improvements.



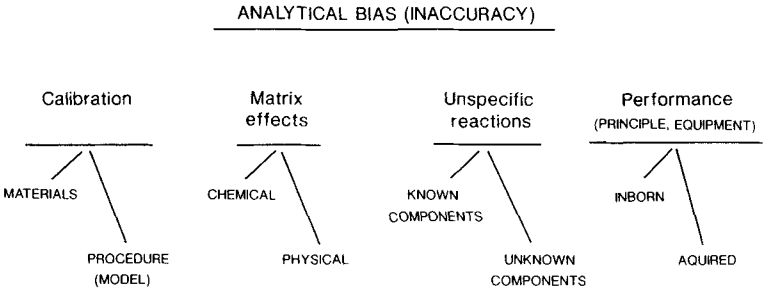
From the clinicians point of view the sources of variations and errors may seem less interesting, but for clinical chemists the splitting up of analytical variation and errors into random and systematic deviation is important. This will give the key for improvements of the quality, and by deviding the systematic deviation into bias (the common deviation from the 'conventional true value' during stable performance) and systematic error (the common deviation from accepted bias in the Laboratory) the possibilities for improving quality are reformed.

Analytical imprecision is mainly determined by the analytical principle (e.g. RIA), pipetting and the equipment (e.g. photometer). Today many instruments meet most requirements for imprecision. This fact, however, does not help the problem with systematic error and bias. Systematic error may be intermittent (e.g. occational wrong performance) or persistent (e.g. batch-to-batch variations in kits). The bias is often caused by poor standardization or unspecific methods.

The analytical quality specifications are different for

monitoring, imprecision and systematic errors are the main factors to be considered, whereas bias (and persistant systematic error) is determining in screening and diagnostics - and when general recommendations are specified for monitoring in relation to a fixed concentration.

Unspecific reactions and matrix effects are often ignored in the specifications of required quality. These factors will also be overlooked in the majorities of control programmes, but they are important and may result in considerable errors, especially in specimens with extreme compositions.



The unspecific reactions are different from component to component so they should be specified for each analytical component, e.g. for S-Triiodothyronine it should be specified that a S-Thyroxine concentration of 200 nmol/L was not allowed to increase the S- Triiodothyronine result by more than 0.1 nmol/L.

The analytical quality specifications should therefore, contain a list og maximum allowable

1) imprecision
2) systematic error
3) bias (mainly standardization)
4) matrix effects (specified)
5) unspecific reactions (specified).

Models for evaluation of imprecision, systematic error, and bias are available (3,4,5), but they should be reinvestigated in order to clearify whether they are still valid or they should be improved. Moreover, models for matrix effects and for unspecific reactions should be developed in this project on 'medical need for quality specifications in laboratory medicine'.

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